

## SHORT COMMUNICATION

## Giant Condyloma Acuminatum in the Axilla

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Condylomata acuminata (CA) are sexually transmitted benign warty lesions that usually affect the anogenital epithelium. Low-risk human papillomavirus (HPV) infection, such as HPV type 6 or 11, is associated with the disease (1). These lesions exhibit a small papular, filiform or cauliflower-like appearance and occasionally grow to be large tumours. Large lesions are often referred to as giant condylomata acuminata (GCA), however, these lesions do not always show locally destructive, aggressive growth, similar to the GCA of Buschke and Löwenstein. GCA usually arise from genital areas, and extra-anogenital GCA is very rare. We herein report a case of GCA in the axilla associated with low-risk HPV type 11 infection.

## CASE REPORT

A 44-year-old man noted a small nodule in the left axilla 3 months prior to admission that had slowly increased in size. The patient had a medical history of dilated cardiomyopathy, cerebral infarction and diabetes mellitus. Furthermore, he had been treated for genital warts 2 years previously. He did not have a significant family history. A physical examination revealed a 35 × 17 mm brownish nodule in the left axilla (Fig. 1a).

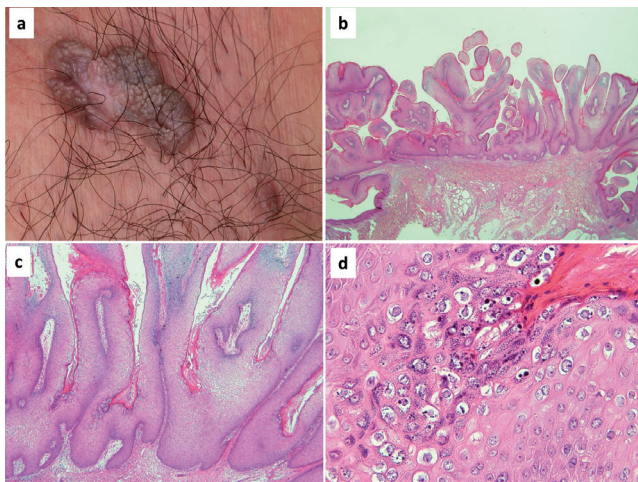


Fig. 1. Clinical appearance and histopathological findings. (a) 35 × 17 mm and 5 × 3 mm brownish nodules in the patient's left axilla. (b) Low-power view showing hyperkeratosis, acanthosis and marked papillomatosis (H&E stain, original magnification × 20). (c) High-power view of the same section showing marked papillomatosis. Elongated rete ridges with flat bottoms were seen. Some parts of the rete ridges looked clear (H&E stain, original magnification × 100). (d) High-power view of the same section showing a slightly disorderly arrangement of keratinocytes and koilocytosis without atypia (H&E stain, original magnification × 400).

A 5 × 3 mm brownish nodule was also seen next to the nodule. Histopathological studies of a skin biopsy specimen obtained from the larger nodule showed epidermal hyperplasia and papillomatosis, suggestive of verrucous carcinoma or seborrhoeic keratosis. We resected the nodule under local anaesthesia, and a histopathological examination revealed marked hyperkeratosis, parakeratosis and papillomatosis (Fig. 1b). The bottom of the rete ridges was flat and parallel to the epidermis (Fig. 1c). No inward proliferation was noted. Koilocytosis was observed in many areas without nuclear atypia (Fig. 1d). Routine laboratory tests revealed no abnormalities. Antibodies against HIV, HCV and HBV were negative. The patient was diagnosed as having GCA in the axilla. There has been no recurrence for one year.

Because the histopathological examination showed many koilocytes in the epidermis, we performed PCR to detect human papillomavirus (HPV). The resected specimen was fixed in 10% neutralised buffered formalin and embedded in paraffin wax. Formalin-fixed, paraffin-embedded samples were then cut into 10 µm sections. After obtaining the patient's informed consent, DNA was extracted from the sections using Dexpat<sup>®</sup> (Takara, Kyoto, Japan). The method and PCR conditions have been previously described (2). HPV PCR was performed with the L1C1/L1C2 consensus primers (2, 3). DNA extracted from a Bowen's disease specimen obtained from another patient, in which HPV type 56 was detected, was used as a control (2). The amplified PCR products were electrophoresed on 2% agarose gel, and a PCR band was seen at the expected position of approximately 250 bp (Fig. 2a). The PCR products were subjected to direct DNA sequencing, which revealed that their sequences

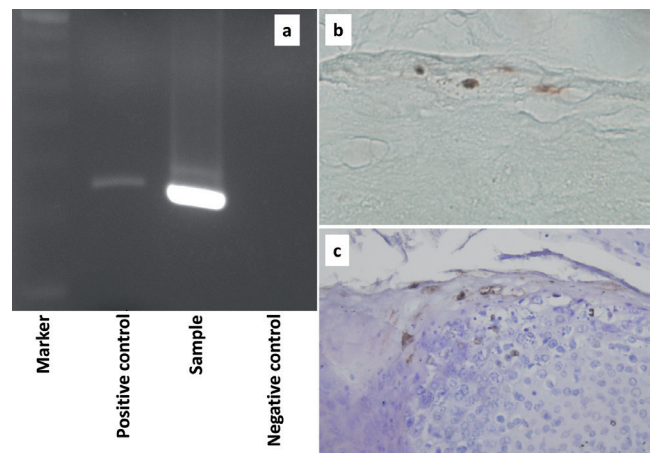


Fig. 2. Detection of human papillomavirus (HPV) DNA on PCR and its localisation in the lesion. (a) HPV DNA was detected on PCR using L1C1/L1C2 consensus primers. The positive control was a sample of HPV type 56, which can be amplified by L1C1/L1C2 consensus primers. The positive control (DNA of HPV type 56) and sample were extracted from formalin-fixed, paraffin-embedded samples. (b) HPV DNA was detected in the nuclei of the epithelium using *in situ* hybridisation. (c) Immunohistochemistry using an anti-HPV antibody (K1H8; Dako) demonstrated HPV capsid proteins in the upper epithelium. Original magnification: (b), (c) × 100.

corresponded to the L1 gene of HPV 11 (data not shown). In order to exclude any co-infection with other HPV types, the PCR products were purified and cloned into a pGEM<sup>®</sup>-T Easy vector (Promega, Madison, WI, U.S.A.) and transfected into *Escherichia coli*. The PCR products cloned into the vectors were sequenced with an automated sequencer. Eight colonies were selected and subjected to DNA sequencing. All sequencing data obtained from each colony were identical to that of HPV type 11. We subsequently performed *in situ* hybridisation using the catalysed signal amplification method (GenPoint System; Dako, Kyoto, Japan) (2). The probe was a HPV Types 6/11 biotinylated DNA probe (GenPoint HPV; Dako). HPV 11 positive cells with nuclear staining were observed in the upper epidermis and stratum corneum (Fig. 2b). Immunohistochemistry was also performed using an anti-HPV antibody (K1H8; Dako) and the avidin-biotin complex method, which revealed that the viral proteins were localised in the upper epidermis and stratum corneum (Fig. 2c).

## DISCUSSION

CA usually manifests as multiple papillomatous lesions; however, several unusual clinical manifestations have been reported, i.e. CA with pigmented papular lesions (4), pigmented plaque-type CA (5), GCA of Buschke and Löwenstein and GCA of the benign type. Among these lesions, GCA of Buschke and Löwenstein is a locally destructive tumour that arises in the anogenital region and is considered to be a variant of verrucous carcinoma. Benign extra-anogenital GCA is rare, with only 3 cases having been reported thus far. Googe et al. (6) reported a healthy 26-year-old pregnant woman who presented with a 6-cm GCA in her left inframammary fold. The lesion was surgically excised, and *in situ* hybridisation revealed that the tumour harboured HPV types 6 and 11. Gupta et al. (7) reported a 50-year-old healthy Indian man with a 5 × 7 cm intraoral GCA. Surgical excision was performed, however, no description of HPV infection was provided. Zhu et al. (8) reported a 30-year-old Chinese man who presented with axillary giant warts. The patient also had a 10-year history of numerous papules and macules on his face, upper trunk and limbs, which ultimately led to the diagnosis of epidermodysplasia verruciformis (EV). HPV type 11 was detected in the giant warts on PCR. Interestingly, HPV type 11 has not previously been reported to be related to EV-HPV which includes HPV types 5, 8, 9, 12, 14, 15, 17, 19, 25, 36, 38, 47 and 50 (9). The authors stated that the abnormality in cell-mediated immunity observed in their case may have been associated with HPV type 11 infection and the subsequent progression of the giant warts. Some similarities exist in the

reported cases of extra-anogenital GCA, including the present case. Three of the 4 patients were HPV type 11 positive, suggesting that HPV type 11 may play a role in the development of extra-anogenital GCA. The sites of development were in moist areas in all cases, with GCA arising in intertriginous regions in 3 of 5 cases. Recently, we reported a case of oncogenic HPV type 56 positive GCA of the groin (10). In that case, oncogenic HPV may have played a role in the formation of the GCA. Why the present patient developed a large tumour is unclear. Because our patient previously had genital warts, they could have caused the lesion in the axilla by autoinoculation. Although we subcloned the PCR products and checked the sequences of the 8 PCR clones, we were unable to exclude the possibility of co-infection with other HPVs. Furthermore, host immunity, the infected HPV type or mutations and the tumour site may partly account for this phenomenon.

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